```
=> d his

     (FILE 'HOME' ENTERED AT 11:44:43 ON 29 APR 2003)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT' ENTERED AT 11:45:18 ON
     29 APR 2003
L1             0 S JANUSBODIES OR JANUSBODY
L2          9463 S JANUS
L3           794 S L2 AND ANTIBOD?
L4             0 S L3 AND (LIGHT CHAIN VARIABL?)
L5             8 S L3 AND VARIABL?
L6             3 DUPLICATE REMOVE L5 (5 DUPLICATES REMOVED)

=>
```

updated search
L/Cook 4/29/03

=> d l6 1-3 all

L6 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
AN 2001697438 MEDLINE
DN 21612718 PubMed ID: 11746271
TI Differential expression of interleukin-15, a pro-inflammatory cytokine and T-cell growth factor, and its receptor in human prostate.
AU Handisurya A; Steiner G E; Stix U; Ecker R C; Pfaffeneder-Mantai S; Langer D; Kramer G; Memaran-Dadgar N; Marberger M
CS Department of Urology, University of Vienna, Vienna, Austria.
SO PROSTATE, (2001 Dec 1) 49 (4) 251-62.
Journal code: 8101368. ISSN: 0270-4137.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200201
ED Entered STN: 20011218
Last Updated on STN: 20020125
Entered Medline: 20020108
AB BACKGROUND: Pro-inflammatory interleukin (IL)-15 plays a major role in host defense and chronic inflammation by stimulating T-lymphocyte recruitment and growth. Expression of IL-15 and IL-15 receptor (IL-15R) in human prostate was examined. METHODS: Normal and benign hyperplastic (BPH) prostate specimens (n = 23) were analyzed for IL-15 and IL-15Ralpha-chain expression by immunohistochemistry and Real-Time-PCR/RT-PCR. Regulation of prostatic stromal cell (PSC) IL-15 mRNA and effect of IL-15 on prostatic cell growth were analysed in vitro. RESULTS: In normal prostate, anti-IL-15 and anti-IL-15Ralpha-chain reactivity were restricted to smooth muscle and stromal cells. However, in BPH, in addition epithelial cells frequently exhibited discrete anti-IL-15R and often intense, membranous anti-IL-15 reactivity. IL-15/IL-15R mRNA were detected in all prostatic cells types. In BPH tissues, IL-15 mRNA content was **variable** (15-fold). IL-15 mRNA synthesis of PSC was significantly up-regulated by IFN-gamma. Furthermore IL-15 strongly stimulated the growth of BPH-T-lymphocytes and weakly that of carcinoma cell lines, but not of stromal cells. CONCLUSIONS: Overexpression of IL-15 and IL-15Ralpha-chain in BPH and massive proliferation of BPH-T-lymphocytes induced by IL-15 suggest a role for IL-15 in prostatic inflammation. Since IFN-gamma, a T-lymphocyte product, stimulates prostatic IL-15 production; chronic inflammation might be triggered by this paracrine loop.

CT Check Tags: Comparative Study; Human; Male; Support, Non-U.S. Gov't
Adolescent
Adult
Cell Division: DE, drug effects
Cell Division: PH, physiology
DNA, Complementary: CH, chemistry
Fluorescent Antibody Technique
Gene Expression Regulation, Neoplastic
Immunohistochemistry
Interleukin-15: AN, analysis
*Interleukin-15: BI, biosynthesis
*Prostate: ME, metabolism
Prostate: PA, pathology
*Prostatic Hyperplasia: ME, metabolism
Prostatic Hyperplasia: PA, pathology
Prostatic Neoplasms: ME, metabolism
Prostatic Neoplasms: PA, pathology
Protein-Tyrosine Kinase: BI, biosynthesis
Protein-Tyrosine Kinase: GE, genetics
RNA, Messenger: BI, biosynthesis
RNA, Messenger: GE, genetics

Receptors, Interleukin-2: AN, analysis
*Receptors, Interleukin-2: BI, biosynthesis
Reverse Transcriptase Polymerase Chain Reaction
Statistics, Nonparametric
Tumor Cells, Cultured

CN 0 (DNA, Complementary); 0 (Interleukin-15); 0 (RNA, Messenger); 0 (Receptors, Interleukin-2); 0 (interleukin-15 receptor); EC 2.7.1.- (**Janus** kinase 1); EC 2.7.1.112 (Protein-Tyrosine Kinase)

L6 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1998:296485 BIOSIS
DN PREV199800296485
TI Combination of interleukin-6 and soluble interleukin-6 receptors induces differentiation and activation of JAK-STAT AND MAP kinase pathways in MG-63 human osteoblastic cells.
AU Nishimura, Riko; Moriyama, Keiji; Yasukawa, Kiyoshi; Mundy, Gregory R.; Yoneda, Toshiyuki (1)
CS (1) University Texas Health Sci. Cent. San Antonio, Dep. Med./Endocrinol., 7703 Floyd Curl Dr., San Antonio, TX 78284-7877 USA
SO Journal of Bone and Mineral Research, (May, 1998) Vol. 13, No. 5, pp. 777-785.
ISSN: 0884-0431.
DT Article
LA English
AB Studies on the role of interleukin-6 (IL-6) in bone metabolism have been accumulating. However, its effects on osteoblasts are still unclear because the results are conflicting depending on the study models employed. We reasoned that these conflicting data are due to **variable** expression levels of membrane-bound IL-6 receptors (IL-6Rs). In the present study, we found that IL-6 in combination with soluble IL-6R (sIL-6R) consistently caused a marked elevation of alkaline phosphatase and a decrease in proliferation in the human osteoblastic cell line MG-63, which expressed no detectable membrane-bound IL-6R and failed to respond to IL-6. These effects of IL-6/sIL-6R were blocked by neutralizing **antibodies** to the IL-6 signal transducer gp130, suggesting an involvement of IL-6 signaling in the elicitation of the effects of IL-6/sIL-6R. Upon stimulation with IL-6/sIL-6R, the gp130, cytoplasmic **Janus** kinases JAK1 and JAK2 were tyrosine phosphorylated. Moreover, signal transducers and activators of transcription STAT1 and STAT3 were also tyrosine phosphorylated, translocated to the nucleus, and bound to the putative STAT-binding DNA elements. In addition, mitogen-activated protein (MAP) kinase was also activated in response to IL-6/sIL-6R. These data demonstrate that sIL-6R may enhance the responsiveness of MG-63 cells to IL-6. Thus, IL-6 in collaboration with sIL-6R may modulate differentiation and proliferation of osteoblastic cells, presumably by activating two distinct signaling pathways of JAK-STAT and MAP kinase.
CC Biochemical Studies - General *10060
Enzymes - General and Comparative Studies; Coenzymes *10802
Metabolism - Metabolic Disorders *13020
Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods *18001
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Skeletal System (Movement and Support)
IT Chemicals & Biochemicals
gp130; interleukin-6; soluble interleukin-6 receptor; JAK: activation, differentiation; MAP kinase: activation, differentiation; STAT: activation, differentiation
IT Miscellaneous Descriptors
bone metabolism
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
MG-63 (Hominidae): human osteoblastic cells
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 9031-44-1 (KINASE)
9026-43-1 (PROTEIN KINASE)
42013-48-9 (GP130)

L6 ANSWER 3 OF 3 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 96194279 EMBASE
DN 1996194279
TI Differential utilization of **Janus** kinase-signal transducer and activator of transcription signaling pathways in the stimulation of human natural killer cells by IL-2, IL-12, and IFN-.alpha..
AU Yu C.-R.; Lin J.-X.; Fink D.W.; Akira S.; Bloom E.T.; Yamauchi A.
CS Div. of Cellular and Gene Therapies, Ctr. for Biologics Evaluation/Res., Food and Drug Administration, 8800 Rockville Pike,Bethesda, MD 20892, United States
SO Journal of Immunology, (1996) 157/1 (126-137).
ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
AB IL-2-, IL-12-, and IFN-.alpha.-mediated signaling pathways were analyzed in primary NK cells and in the NK3.3 cell line. Gel mobility shift and immunoprecipitation analyses revealed that in addition to activating STAT3 (signal transducer and activator of transcription-3) and STAT5, IL-2 induced tyrosine and serine phosphorylation of STAT1.alpha., which formed IFN-.gamma.-activated sequence-binding complexes by itself and with STAT3. Although IL-2 and IFN- .alpha. activated STAT1.alpha. and STAT5, IL-2 predominantly activated STAT5, while IFN-.alpha. predominantly activated STAT1.alpha.. IL-2 induced less STAT1.alpha. activation and IFN-.alpha. induced greater STAT5 activation in NK3.3 cells compared with preactivated primary NK cells. In NK3.3 cells, IL-2 induced comparable formation of c-fos promoter sis-inducible element IFN-.gamma.-activated sequence-binding complexes containing STAT3 alone with complexes containing STAT3 and STAT1.alpha., while in preactivated primary NK cells, it preferentially induced complexes containing STAT3 and STAT1.alpha.. Thus, signaling in NK3.3 cells is not always identical with that in primary NK cells. In contrast to IL-2 and IFN- .alpha., IL-12 induced strong tyrosine phosphorylation of STAT4 and **variable** weak phosphorylation of STAT3. However, supershift analyses using the c-fos promoter sis-inducible element probe showed that IL-12 activated STAT4, STAT1.alpha., and STAT3, and induced complexes containing STAT4 only, STAT4 with STAT1.alpha., STAT3 with STAT1.alpha., or STAT1.alpha. only in preactivated primary NK cells. STAT1.alpha. activation by IL-12 correlated with increased phosphorylation of serine, but not tyrosine. Finally, IL-2 induced tyrosine phosphorylation of JAK1 and JAK3, while IL-12 induced phosphorylation of JAK2 and TYK2 in both preactivated primary NK and NK3.3 cells. Differential phosphorylation and consequent differential activation of both separate and overlapping STAT proteins by IL-2, IL-12, and IFN-.alpha. may provide a molecular basis for the similarities and differences in the actions of these cytokines on NK cells.
CT Medical Descriptors:
*immunoregulation
*natural killer cell
*t lymphocyte activation
antigen antibody complex
article
human
human cell
oncogene c fos

priority journal
promoter region
protein phosphorylation
signal transduction
transcription initiation
Drug Descriptors:
*alpha interferon
*interleukin 12
*interleukin 2
transcription factor
RN (interleukin 12) 138415-13-1; (interleukin 2) 85898-30-2

=> d hsi
'HSI' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> d his

(FILE 'HOME' ENTERED AT 11:44:43 ON 29 APR 2003)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT' ENTERED AT 11:45:18 ON
29 APR 2003
L1 0 S JANUSBODIES OR JANUSBODY
L2 9463 S JANUS
L3 794 S L2 AND ANTIBOD?
L4 0 S L3 AND (LIGHT CHAIN VARIABL?)
L5 8 S L3 AND VARIABL?
L6 3 DUPLICATE REMOVE L5 (5 DUPLICATES REMOVED)

=>

(FILE 'HOME' ENTERED AT 12:06:30 ON 29 APR 2003)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 12:07:08 ON 29 APR 2003

```
L1          6478 S (BENCE JONES PROTEIN)
L2             0 S L1 AND (PEPTIDE LINKER)
L3           662 S L1 AND PEPTIDE?
L4             4 S L3 AND LINKER?
L5             1 DUPLICATE REMOVE L4 (3 DUPLICATES REMOVED)
L6            36 S (COMPLEMENTARITY DETERMINING SEGMENTS)
L7            10 S L6 AND PEPTIDE?
L8             0 S L6 AND LINKER?
L9             6 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)
L10          776 S (PEPTIDE LINKER)
L11          344 S L10 AND ANTIBOD?
L12            4 S L11 AND CDR?
L13            1 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
```

=>

updated search LY Cook 4/29/03

```
 (FILE 'HOME' ENTERED AT 12:06:30 ON 29 APR 2003)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
     12:07:08 ON 29 APR 2003
L1          6478 S (BENCE JONES PROTEIN)
L2             0 S L1 AND (PEPTIDE LINKER)
L3           662 S L1 AND PEPTIDE?
L4             4 S L3 AND LINKER?
L5             1 DUPLICATE REMOVE L4 (3 DUPLICATES REMOVED)
L6            36 S (COMPLEMENTARITY DETERMINING SEGMENTS)
L7            10 S L6 AND PEPTIDE?
L8             0 S L6 AND LINKER?
L9             6 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)
L10          776 S (PEPTIDE LINKER)
L11          344 S L10 AND ANTIBOD?
L12            4 S L11 AND CDR?
L13            1 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)

=>
```

L13 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 1993:140733 BIOSIS
DN PREV199395073533
TI Role of mouse V-H10 and VL gene segments in the specific binding of **antibody** to Z-DNA, analyzed with recombinant single chain Fv molecules.
AU Brigido, Marcelo M.; Polymenis, Michael; Stollar, B. David (1)
CS (1) Dep. Biochem., Tufts Univ. Sch. Med., 136 Harrison Ave., Boston, MA 02111 USA
SO Journal of Immunology, (1993) Vol. 150, No. 2, pp. 469-479.
ISSN: 0022-1767.
DT Article
LA English
AB A plasmid vector was constructed for the expression of a single chain Fv domain of mouse mAb to Z-DNA (**antibody** Z22), which is encoded by V-H10 and V-kappa-10 gene family members along with Dsp2, J-H4, and J-K4 segments. The vector coded for a PhoA secretion signal, VH segment, flexible **peptide linker**, VL segment, (His)-5, and a protein A domain. Unique restriction sites allowed exchange of the segments as cassettes. Bacteria transformed with the vector secreted soluble recombinant Fv with specific Z-DNA-binding activity. When the L chain of Z22 was replaced with a library of splenic VL cDNA from a mouse immunized with Z-DNA, only a light chain closely resembling that of the original Z22 (differing at six amino acid positions) yielded Fv with Z-DNA-binding activity. The Fv with this L chain replacement had a lowered affinity, but remained selective for Z-DNA. Replacement of the Z22 H chain with a mixture of 11 V-H10-encoded H chains yielded two Z-DNA binding clones, but they bound B-DNA and denatured DNA as well as Z-DNA. The replacement clones indicate the importance of the H chain **CDR3** and particular VH-VL combinations in formation of specific **antibodies** to Z-DNA.
CC Genetics and Cytogenetics - Animal *03506
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Immunology and Immunochemistry - General; Methods *34502
BC Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Genetics; Immune System (Chemical Coordination and Homeostasis); Methods and Techniques
IT Chemicals & Biochemicals
Z-DNA
IT Sequence Data
amino acid sequence; molecular sequence data
IT Miscellaneous Descriptors
GENETIC ENGINEERING; HEAVY CHAIN; LIGHT CHAIN; REPLACEMENT CLONES; RESTRICTION SITES; VECTOR CONSTRUCTION; Z22 **ANTIBODY**
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Muridae (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates
RN 121182-96-5 (Z-DNA)

=>

L9 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1977:550064 CAPLUS
DN 87:150064
TI Unusual distributions of amino acids in complementarity-determining (hypervariable) segments of heavy and light chains of immunoglobulins and their possible roles in specificity of antibody-combining sites
AU Kabat, Elvin A.; Wu, Tai Te; Bilofsky, Howard
CS Natl. Cancer Inst., NIH, Bethesda, MD, USA
SO Journal of Biological Chemistry (1977), 252(19), 6609-16
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB Using a data bank of sequence of variable regions of immunoglobulin chains to compute incidences of the 20 amino acids at various positions in the **complementarity-detg. segments** of light and heavy chains, it was possible to infer that certain amino acids at 13 positions in the light chain and 7 positions in the heavy chain functioned in antibody-combining sites as structural elements rather than as contacting or conformationally important residues. These inferences are in good agreement with assignments made by x-ray crystallog. in almost all instances. The statistical method, however, is independent of x-ray crystallog. and may permit assigning a role to a position or to a given amino acid at a position in many kinds of antibody-combining sites, while an x-ray structure provides information only about the antibody being studied. The role of individual amino acids at various positions is greatly affected by insertions or deletions in the **complementarity -detg. segments**. The method also permits one to infer that particular amino acids in **complementarity-detg. segments** such as histidine and tryptophan are either directly involved in specificity as contacting residues, or exert a conformational influencee on such residues. The findings indicate the need for x-ray crystallog. studies on immunoglobulins with insertions of different lengths in complmentarity-detg. segments and with sites shown from immunochem. consideration to be grooves or cavities.
ST computer application Ig amino acid; conformation Ig amino acid position; Ig variable sequencee structure site; amino acid distribution complementarity Ig
IT Immunoglobulins
RL: BIOL (Biological study)
(amino acid distribution in complementarity-detg. secments of)
IT **Peptides**, properties
RL: PRP (Properties)
(amino acid sequences of, of Ig, **complementarity-detg . segments** in relation to)
IT Amino acids, biological studies
RL: BIOL (Biological study)
(of Ig, in **complementarity-detg. segments**)
IT 71-00-1, biological studies 73-22-3, biological studies
RL: BIOL (Biological study)
(of Ig, in **complementarity-detg. segments**)

L9 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1976:72525 CAPLUS
DN 84:72525
TI Similarities among hypervariable segments of immunoglobulin chains
AU Wu, Tai Te; Kabat, Elvin A.; Bilofsky, Howard
CS Dep. Eng. Sci., Northwest. Univ., Evanston, IL, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1975), 72(12), 5107-10
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB A human .lambda.V (Meg) and a human .lambda.II (Vil) myeloma protein have identical sequences in their first hypervariable segments although they differ at 21 positions throughout the variable region. If a diferent structural gene is responsible for each subgroup, the findings favor insertion of information for the hypervariable or **complementarity -detg. segments.**
ST immunoglobulin **peptide** gene
IT Globulins, immune
RL: BIOL (Biological study)
(myeloma Mcg and Vil, amino acids and **peptides** of, gene in relation to)
IT Amino acids, biological studies
Peptides, biological studies
RL: BIOL (Biological study)
(of immunoglobulins, gene in relation to)

L9 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1976:72525 CAPLUS
DN 84:72525
TI Similarities among hypervariable segments of immunoglobulin chains
AU Wu, Tai Te; Kabat, Elvin A.; Bilofsky, Howard
CS Dep. Eng. Sci., Northwest. Univ., Evanston, IL, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1975), 72(12), 5107-10
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB A human .lambda.V (Meg) and a human .lambda.II (Vil) myeloma protein have identical sequences in their first hypervariable segments although they differ at 21 positions throughout the variable region. If a diferent structural gene is responsible for each subgroup, the findings favor insertion of information for the hypervariable or **complementarity -detg. segments**.
ST immunoglobulin **peptide** gene
IT Globulins, immune
RL: BIOL (Biological study)
(myeloma Mcg and Vil, amino acids and **peptides** of, gene in relation to)
IT Amino acids, biological studies
Peptides, biological studies
RL: BIOL (Biological study)
(of immunoglobulins, gene in relation to)